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October 4, 2011

VIA ECF & FEDEX

TO: Magistrate Judge Patty Shwartz
Martin Luther King, Jr. Federal Building & U.S. Courthouse
50 Walnut Street
Newark, NJ 07101

Re: *Prometheus Laboratories Inc. v. Roxane Laboratories, Inc.*,
Civil Action No. 11-1241 (FHS)(PS)

Dear Judge Shwartz:

This firm, together with Goodwin Procter, represents Defendant Roxane Laboratories, Inc. ("Roxane") in the above captioned matter. Roxane opposes Plaintiff Prometheus Laboratories Inc.'s ("Prometheus") request for leave to amend Prometheus's complaint[1] to add: (1) Cipla, Ltd. ("Cipla") and Byron Chemical Co., Inc. ("Byron") as Defendants; and (2) allegations that Roxane, Cipla and Byron infringe non Orange Book listed[2] U.S. Patent No. 6,175,014 ("the '014 patent"). The '014 patent is directed to a process for making alosetron active pharmaceutical ingredient ("API"). That patent is unrelated to the patent that Prometheus originally asserted – Orange Book listed U.S. Patent No. 6,284,770 ("the '770 patent") – which claims a method for administering alosetron to a subpopulation of irritable bowel syndrome ("IBS") patients. Prometheus's new allegations should be dismissed because: (1) they are futile,

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1 Prometheus only seeks leave to amend its complaint in Civ. No. 11-1241 and not in Civ. No. 11-0230.

2 The "Orange Book" is the United States Food & Drug Administration ("FDA") publication titled "*Approved Drug Products with Therapeutic Equivalence Evaluations*," which lists the patent number and expiration date of any patent that a New Drug Application ("NDA") filer identifies to the FDA as claiming the drug (in the NDA filing) or a method of using the drug with respect to which a claim of patent infringement could reasonably be asserted.

as Prometheus should have discovered through an appropriate prefiling investigation; and (2) they are untimely. Granting Prometheus's request for leave would severely prejudice Roxane and unduly delay the resolution of the present action. As early as May 2011 Prometheus knew about the process used to make the alosetron used in Roxane's allegedly infringing products and knew that Cipla manufactured that API, yet Prometheus waited until now, four months later, to seek leave to amend.

I. INTRODUCTION

In March 2011 Prometheus filed a Complaint alleging that Roxane infringed the '770 Orange Book patent by filing an Abbreviated New Drug Application ("ANDA") that seeks FDA approval to sell a generic version of Prometheus's LOTRONEX® tablets ("Roxane's ANDA products"). LOTRONEX® tablets are indicated for the treatment of IBS. On May 17, 2011, Roxane produced its ANDA to Prometheus. On June 3, 2011, the Court set specific discovery deadlines. Discovery is ongoing. The parties are working to resolve issues regarding discovery that Roxane seeks from Prometheus and from non-party GlaxoSmithKline ("GSK"). Moreover, the deadline for filing Hague Requests is this Thursday (October 6), infringement and invalidity contentions have already been served, and proceedings to construe terms in the claims of the '770 patent are underway.

A. The Court Should Not Add The Non Orange Book Listed '014 Patent To This Litigation

Roxane's ANDA products incorporate alosetron API manufactured by Cipla. Roxane's ANDA references Cipla's Drug Master File No. 22125 for alosetron API ("the Cipla DMF"). That DMF was filed with the FDA and provides detailed information regarding Cipla's process for manufacturing alosetron API ("the Cipla process"). The Cipla DMF has two portions: (1) a portion containing confidential company information that is not intended for purchasers of Cipla's API made by the Cipla process and is provided to the FDA to permit a complete evaluation of the API and the API manufacturing process; and (2) a portion containing the confidential information that may be provided to API purchasers. These portions are often referred to as the "Closed Portion" and the "Open Portion," respectively. Roxane's ANDA includes only the Open Portion of the Cipla DMF and tells the FDA the source of Roxane's API. The FDA uses the complete Cipla DMF for its review and approval of the Cipla API.

On September 13, 2011, Prometheus informed Roxane that Prometheus planned to seek leave to amend its complaint to add, *inter alia*, allegations of infringement of the non Orange Book listed '014 patent. The allegations of infringement of the '014 patent in Prometheus's proposed amended complaint are based *solely* on information obtained from the Open Portion of the Cipla DMF found in Roxane's ANDA. Roxane produced that information to Prometheus over four months before Prometheus informed Roxane that Prometheus planned to seek leave to amend its complaint based on that information.

After learning that Prometheus planned to seek leave to amend its Complaint to add allegations of infringement of the non Orange Book listed '014 patent, counsel for Roxane investigated those allegations. (Zullow Decl., ¶¶ 3, 6.[3]) As part of that investigation, counsel for Roxane entered into a confidentiality agreement with Cipla so that counsel for Roxane could see the complete API process information that is included in the Closed Portion of the Cipla DMF but not in the Open Portion found in Roxane's ANDA. (Zullow Decl., ¶ 6.) Counsel for Roxane informed Prometheus, both before and after Prometheus requested leave to amend, that Prometheus should view the detailed process information in the Closed Portion of the Cipla DMF – information that was not included in Roxane's ANDA – before reaching any conclusions about whether the Cipla process infringed any claim of the '014 patent. (Zullow Decl., ¶¶ 7-9; Zullow Decl., Exs. C and D.) Counsel for Roxane also provided information to counsel for Prometheus from which counsel for Prometheus could conclude that the Cipla process ***does not*** infringe any claim of the '014 patent. (Zullow Decl., ¶¶ 7-9; Zullow Decl., Exs. A, C and D.)

More specifically, the '014 patent claims a process for making alosetron API. The claimed process includes the step of reacting a compound of formula (II) (as defined in the '014 patent) with a compound of formula (III). (Zullow Decl., Ex. E at 6:55-7:36.) The '014 patent defines the compound of formula (III) as an alcohol (-OH) containing imidazol. (*Id.* at 7:28-31.**)** Counsel for Roxane informed counsel for Prometheus, by telephone and by letter, that:

(a) [redacted];

(b) [redacted];

(c) Cipla had indicated a willingness to enter into a confidentiality agreement with outside counsel for Prometheus so that outside counsel for Prometheus could view detailed process information contained in the Closed Portion of the Cipla DMF (which is not in the Open Portion of the DMF found in Roxane's ANDA); and

(d) if Prometheus delayed the filing of its motion for leave to amend to further investigate its allegations of infringement of the '014 patent, Roxane would not use that delay as a basis to oppose a later filed motion for leave to amend.

(Zullow Decl., ¶¶ 7-9; Zullow Decl., Exs. C and D.)

[3] Zullow Decl., ¶ __ and Zullow Decl., Ex. __ refer respectively to the corresponding paragraph of or exhibit attached to the Declaration of Keith A. Zullow In Support Of Roxane's Letter In Opposition To Prometheus's Request For Leave To File An Amended Complaint.

On information and belief, despite having the above information before filing its request for leave to amend, Prometheus has not contacted Cipla to obtain any additional information about the Cipla process. Indeed, the bare-boned unsupported allegations in Prometheus's proposed amended complaint ignore that information:

> On information and belief, Cipla's DMF No. 22125 describes a process for manufacturing alosetron hydrochloride API that will infringe one or more claims of the '014 patent if Cipla's API is shipped into the United States before the expiration of the '014 patent.

(D.I. No. 38, Ex. A at ¶ 34.) In addition to the fact that Prometheus did not complete a reasonable prefiling investigation, Prometheus's unsupported legal conclusions regarding infringement do not even meet Rule 12(b)(6) standards. For these reasons alone, Prometheus's allegations of infringement of the '014 patent are futile, and Prometheus's request for leave to amend its Complaint to add those allegations should be denied.

Prometheus's proposed amendment is also futile because the Court lacks subject matter jurisdiction over a claim for infringement of the '014 patent. The FDA has not approved Roxane's request to sell a generic version of LOTRONEX®, and cannot approve that request before the January 13, 2013 expiration of Prometheus's Orange Book listed U.S. Patent No. 5,360,800 ("the '800 patent"), which claims the compound alosetron. Roxane therefore cannot infringe the '014 patent until some undetermined date no earlier than January 13, 2013.

B. The Court Should Not Add Cipla And Byron To This Litigation

Cipla and Byron should not be added as parties at this late date with respect to the '770 patent. Prometheus's allegation of infringement of the '770 method of use patent centers on the labeled instructions for the method of using Roxane's alosetron ANDA product; not the composition or process of making Roxane's alosetron ANDA product. Roxane controls the proposed labeling, not Cipla or Byron. There is no relevant discovery that is needed from Cipla or Byron. Prometheus alleges that Cipla and Byron will contributorily infringe the '770 patent by supplying alosetron API to Roxane. However, there can be no contributory infringement until there is a sale of the finished drug product, which will only occur, at the earliest, after January 13, 2013 when the Orange Book listed '800 patent expires. There is no legitimate need for Cipla and Byron to be added as parties to this lawsuit. Adding those parties will interfere with Roxane's relationship with its supplier, unduly complicate this case, add extra, unnecessary expense and delay the proceedings.

C. Prometheus's Late-Filed Proposed Amendment Is Nothing More Than An Attempt To Delay And Will Unduly Prejudice Roxane

Prometheus's undue delay in seeking leave to amend also warrants denial of its request. Prometheus received the Cipla process information underlying Prometheus's allegations of

infringement of the '014 patent about four months ago, yet only sought leave to amend its pleadings 11 days ago. Prometheus's request for leave to amend comes after Roxane served discovery requests focused on the '770 patent on Prometheus and non-party GSK[4], weeks after contentions have been exchanged per the local rules, weeks after claim construction proceedings began, shortly before the deadline to bring discovery issues to this Court and mere days before the deadline for filing Hague Requests. The '014 patent has different named inventors than the '770 patent and claims completely different subject matter than the '770 patent. If the '014 patent is added to the litigation, Roxane will have to serve additional discovery requests on Prometheus and GSK, file another Hague request, serve additional contentions, and additional claim construction proceedings directed to the '014 patent will be necessary.

Moreover, Roxane had proposed, and the Court adopted, a schedule that allowed for a resolution of issues regarding the '770 patent in early 2013. Introducing the '014 patent, the resolution of which concerns completely different issues than the '770 patent, and new parties, who have not even committed any acts that could be considered infringement, may unnecessarily delay trial concerning the '770 patent. There is no need to try issues regarding the '770 patent and the '014 patent in the same litigation.

For these reasons and the reasons discussed further below, Prometheus's request for leave to amend should be denied.

II. ARGUMENT

A. The Pertinent Law

The grant or denial of a motion for leave to amend is within the sound discretion of this Court. *Foman v. Davis*, 371 U.S. 178, 182 (1962). Rule 15(a) provides that "leave shall be freely given ***when justice so requires.***" FED. R. CIV. P. 15(a) (emphasis added). Leave to amend need not be granted when justice does not so require. "Among the factors that may justify denial of leave to amend are undue delay, bad faith, and futility." *Arthur v. Maersk, Inc.*, 434 F.3d 196, 204 (3d Cir. 2006).

A proposed amendment is futile if it "is frivolous or advances a claim or defense that is legally insufficient on its face." *Harrison Beverage Co. v. Dribeck Importers, Inc.*, 133 F.R.D. 463, 468 (D.N.J. 1990) (internal citations and quotation marks deleted). A motion for leave to amend should also be denied on grounds of futility where the allegations of a complaint fail to demonstrate subject matter jurisdiction. *See Roberts v. Mayor and Burgesses of London Borough of Brent*, 70 Fed. Appx. 615, 619 (3d Cir. 2003) ("[I]t was clear from [the] complaint that the District Court lacked subject matter jurisdiction over his suit. Accordingly, the District Court was not required to grant [] leave to amend.").

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[4] Glaxo Group Limited (a British entity now part of GSK) was the original patentee of the '014 patent.

"The question of undue delay, as well as the question of bad faith, requires that we focus on the [moving party's] motives for not amending their [pleading] to assert this claim earlier; the issue of prejudice requires that we focus on the effect on the [non-moving party]." *Adams v. Gould, Inc.*, 739 F.2d 858, 868 (3d Cir. 1984). "[P]rejudice to the non-moving party is the touchstone for the denial of the amendment." *Bechtel v. Robinson*, 886 F.2d 644, 652 (3d Cir. 1989) (quoting *Cornell & Co., Inc. v. Occupational Safety and Health Review Comm'n*, 573 F.2d 820, 823 (3d Cir. 1978)).

Grant of Prometheus's request will severely prejudice Roxane by forcing Roxane to bear added cost and delay to defend against Prometheus's late and futile allegations.

B. Prometheus's Request For Leave To Amend The Complaint To Add Allegations Regarding The '014 Patent Should Be Denied As Futile Because Prometheus Failed To Conduct A Reasonable Prefiling Investigation And Its Pleaded Allegations Are Conclusory And Speculative

Pursuant to Rule 11, Prometheus must have a reasonable basis for asserting infringement of the '014 patent before seeking leave to amend its complaint. A prefiling assessment of the basis of each infringement claim is "extremely important" because "[d]efending against baseless claims of infringement subjects the alleged infringer to undue costs – precisely the scenario Rule 11 contemplates." *View Eng'g, Inc. v. Robotic Vision Sys.*, 208 F.3d 981, 986 (Fed. Cir. 2000).

Prometheus argues that the standard for assessing futility is the same standard of legal sufficiency that applies under Rule 12(b)(6). (D.I. No. 38 at 5.) That argument ignores Prometheus's obligation to conduct a reasonable investigation before seeking leave to amend.

Paragraph 34 of Prometheus's proposed amended complaint is the only allegation that sets forth the basis for Prometheus's allegation that the Cipla process infringes the claims of the '014 patent. Paragraph 34 states:

> ***On information and belief***, Cipla's DMF No. 22125 describes a process for manufacturing alosetron hydrochloride API that will infringe one or more claims of the '014 patent if Cipla's API is shipped into the United States before the expiration of the '014 patent.

(D.I. No. 38, Ex. A at ¶ 34 (emphasis added).) That allegation ignores the information that counsel for Roxane provided to counsel for Prometheus regarding the Cipla process, indicating that Prometheus had a mistaken understanding of the process based on the Open Portion of the Cipla DMF produced as part of Roxane's alosetron ANDA. **(**Zullow Decl., ¶¶ 7-9; Zullow Decl., Exs. A, C and D.) Roxane offered to assist Prometheus in entering a confidentiality agreement with Cipla so that counsel for Prometheus could have access to the Closed Portion of the Cipla DMF and confirm the information that counsel for Roxane had provided regarding the Cipla process. Roxane is not aware of Prometheus having attempted to contact Cipla to further

investigate its allegations of infringement of the '014 patent. A reasonable pre-suit investigation, in which Prometheus followed-up on the information provided by counsel for Roxane, would have demonstrated the futility of Prometheus's request for leave to amend.

Prometheus states that "Roxane has resisted producing documents concerning the manufacture of alosetron used in its proposed product." (D.I. No. 38 at 5.) That statement is inaccurate and misleading for the following reasons. First, Prometheus's discovery requests were made in the context of Prometheus's allegations of infringement of the '770 method of use patent. The '770 patent claims a method of using alosetron to treat a subpopulation of IBS patients; it does not claim or in any way relate to a process for manufacturing alosetron API. Discovery regarding the Cipla API manufacturing process therefore is not relevant to any issue in this case. Second, Roxane does not have any documents within its possession, custody or control regarding the Cipla process other than the Open Portion of the DMF in Roxane's ANDA, which Roxane already has produced. Third, Prometheus completely ignores the additional information that counsel for Roxane provided to counsel for Prometheus after learning of Prometheus's plans to seek leave to amend its Complaint to add allegations of infringement of the '014 patent – information that counsel for Roxane obtained by conducting the kind of investigation regarding the Cipla process that Prometheus could have, and should have, conducted before moving for leave to amend.

Prometheus states: "[redacted]." (D.I. No. 38 at 5.) That statement is inaccurate, misleading and taken out of context. First, Prometheus fails to acknowledge that Roxane's ANDA includes only the Open Portion of Cipla's DMF and that counsel for Roxane informed counsel for Prometheus that the Closed Portion of the Cipla DMF provides the complete process for preparing the API. It is the complete process that is relevant to determining whether or not the Cipla process infringes the '014 patent. Second, even though Roxane's ANDA includes the Open Portion of the Cipla DMF, FDA addresses all DMF issues (and thus API issues) to Cipla, not Roxane, because only Cipla has access to the entire DMF.

Prometheus's proposed amendment is also "legally insufficient on its face." *Harrison Beverage*, 133 F.R.D. at 468. Under a proper Rule 12(b)(6) analysis, a party must set forth "enough facts to state a claim to relief that is plausible on its face." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007). As Your Honor stated:

> Detailed factual allegations are not necessary to survive a Rule 12(b)(6) motion, but "a [pleader's] obligation to provide the grounds of his entitlement to relief requires more than labels[,] … conclusions, and a formulaic recitation of the elements of a cause of action" and demands that the "[f]actual allegations … be enough to raise a right to relief above the speculative level … on the

> assumption that all the allegations in the [pleading] are true (even if doubtful in fact)."

Transweb, LLC v. 3M Innovative Properties Co., Civ. No. 10-4413 (FSH), 2011 WL 2181189, at *9 (D.N.J. June1, 2011) (quoting *Twombly*, 550 U.S. at 555). Your Honor explained that determining whether the Rule 12(b)(6) standard is met requires a two part analysis: (1) separating the factual and legal elements; and (2) determining whether the "complaint articulates 'enough facts to state a claim to relief that is plausible on its face.'" *Id.* at *28 (quoting *Twombly*, 550 U.S. at 570).

Prometheus's proposed amended complaint does not contain factual allegations sufficient to support its legal conclusion that "Cipla's DMF No. 22125 describes a process for manufacturing alosetron hydrochloride API that will infringe one or more claims of the '014 patent if Cipla's API is shipped into the United States before the expiration of the '014 patent." (D.I. No. 38, Ex. A at ¶ 34.) Prometheus's allegations do not address any of the actual process limitations in the claims of the '014 patent. Prometheus could not address those process limitations without acknowledging the Cipla process information provided by counsel for Roxane and the differences between the Cipla process and the process claimed in the '014 patent. Prometheus was left with no choice but to file a proposed amendment that is speculative at best and contains only an "unsupported conclusion" regarding infringement of the '014 patent. *See Schuylkill Energy Res., Inc. v. Pennsylvania Power & Light Co.*, 113 F.3d 405, 417 (3d Cir.1997) (explaining that the Court need not accept as true "unsupported conclusions and unwarranted inferences").

For the above reasons, Prometheus' proposed amendment is futile.[5]

C. Prometheus's Request For Leave To Amend The Complaint Is Futile Because The Court Lacks Subject Matter Jurisdiction

Prometheus bears the burden of proving that subject matter jurisdiction exists. *Mortensen v. First Fed. Sav. & Loan Ass'n*, 549 F.2d 884, 891 (3d Cir. 1997). The Court should deny Prometheus's request for leave because Prometheus cannot meet that burden.

1. There Is No Case Or Controversy With Respect To Prometheus's Allegations That Roxane, Cipla And Byron Infringe The '014 Patent

Prometheus's proposed amended complaint (D.I. No. 38, Ex. A) asserts infringement under Section 271(g) based upon the following allegations:

- Cipla submitted DMF No. 22125 to the FDA on August 18, 2009, and that DMF is directed to the manufacture of Cipla's API (¶ 31);

[5] Roxane reserves the right to request Rule 11 sanctions against Prometheus for requesting leave to amend its Complaint before completing a reasonable investigation.

- [redacted], and Cipla and Byron intend to import and have imported Cipla's API into the U.S. without authority from Prometheus (¶ 32);
- [redacted] (¶ 33); and
- Cipla's DMF describes a process for manufacturing alosetron hydrochloride API that will infringe one or more claims of the '014 patent if Cipla's API is shipped into the United States before the expiration of the '014 patent (¶ 34).

This Court lacks subject matter jurisdiction to address Prometheus's allegations for the following reasons. First, this Court has held, relying on Federal Circuit precedent, "that to establish an act of infringement pursuant to § 271(e)(2), the ANDA must contain a Paragraph IV certification against a patent listed in the Orange Book for the drug in question."[6] *Eisai Co., Ltd. v. Mutual Pharm. Co., Inc.*, Civ. No. 06-3613 (HAA), 2007 WL 4556958, at *12, (D.N.J. Dec. 20, 2007). Section 271(e)(2)(A) "gives rise to only a limited set of statutorily-defined consequences" for a "highly artificial act of infringement." *See Glaxo Group, Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1349 (Fed. Cir. 2004). Section 271(e)(2)(A) states:

> It shall be an act of infringement to submit-- (A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent.

35 U.S.C. § 271(e)(2)(A). The '014 patent is not listed in the Orange Book. 21 C.F.R. § 314.53(b)(1) ("Process patents . . . are not covered by this section, and information on these patents may not be submitted to FDA."). Therefore, an ANDA cannot contain a Paragraph IV certification against the '014 patent, Section 271(e)(2)(A) does not apply, and the filing of Roxane's alosetron ANDA does not constitute an artificial act of infringement of the '014 patent. Prometheus must therefore establish subject matter jurisdiction by some other means. Prometheus has not done so and cannot do so.

Second, there has been no infringing activity under Section 271(g). Activities conducted as part of preparing and filing Roxane's ANDA fall under the safe harbor provision of Section 271(e)(1), which states:

> It shall not be an act of infringement to make, use, offer to sell, or sell within the United States … a patented invention … solely for uses reasonably related to the development and submission of

[6] A Paragraph IV certification is a certification included in an ANDA, pursuant to 35 U.S.C. § 355 (j)(2)(A)(vii)(IV), that a patent is invalid, unenforceable, or would not be infringed by the manufacture, use or sale of the drug product that is the subject of the ANDA.

> information under a Federal law which regulates the manufacture, use, or sale of drugs.

35 U.S.C. § 271(e)(1). Prometheus does not allege that any of Roxane's, Cipla's or Byron's activities fall outside the Section 271(e)(1) safe harbor.

Third, this case does not present a controversy of "sufficient immediacy" between Prometheus and Roxane, Cipla and Byron to award a declaratory judgment under Section 271(g). The Declaratory Judgment Act gives a court discretion to declare the rights and other legal relations of a party seeking such a declaration only in a case of actual controversy. 28 U.S.C. § 2201. A party seeking declaratory relief must prove that "the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *MedImmune, Inc. v Genentech, Inc.*, 549 U.S. 118, 127 (2007). The dispute must be "definite and concrete," and redressable through "a decree of conclusive character, as distinguished from an opinion advising what the law would be upon a hypothetical state of facts." *Janssen Pharmaceutica, N.V. v. Apotex, Inc.*, 540 F.3d 1353, 1360 (Fed. Cir. 2008) (quoting *MedImmune*, 549 U.S. at 127). It must be "based on a real and immediate injury … an objective standard that cannot be met by a purely subjective or speculative fear of future harm." *Prasco, LLC v. Medicis Pharm. Corp.*, 537 F.3d 1329, 1339 (Fed. Cir. 2008). Prometheus bears the burden of proving that subject matter jurisdiction exists. *Mortensen*, 549 F.2d at 891.

Prometheus's allegations involve hypothetical future infringements and do not meet Prometheus's burden of showing a "real and immediate injury." Roxane does not seek approval of its ANDA product until January 2013, fifteen months from now, when the '800 Orange Book patent expires. There can be no infringing activity until Roxane receives that approval. The hypothetical possibility that the FDA may approve Roxane's alosetron ANDA in 15 months and that Roxane may launch an alosetron product using API made by the Cipla process is not sufficient to establish an actual controversy. *See Eisai Co.*, 2007 WL 4556958, at *18 ("The alleged future infringement depends on two contingent future events: FDA approval of Mutual's ANDA, and Mutual's decision to market a generic version of Aricept® ODT pursuant to that ANDA. At least until the ANDA is approved, however, the controversy is not sufficiently immediate."); *Sierra Applied Sciences, Inc. v. Advanced Energy Indus., Inc.*, 363 F.3d 1361, 1379-80 (Fed. Cir. 2004) (declining to find subject matter jurisdiction when the potentially infringing activity would not begin until about a year after the complaint was filed); *In re Rosuvastatin Calcium Patent Litig.*, MDL No. 08-1949, 2008 WL 5046424, at *12-*13 (D. Del. Nov. 24, 2008) (finding that there was no actual controversy sufficient to create subject matter jurisdiction when FDA approval, and the first potential infringement, was possible in approximately 18 months).

For these additional reasons, Prometheus's request for leave to amend its Complaint to add allegations of infringement of the '014 patent is futile and should be denied.

2. Section 271(e)(2)(A) Does Not Confer Jurisdiction Over Prometheus's Allegation That Cipla And Byron Infringe The '770 Patent

Under Section 271(e)(2)(A), an infringement suit can only be filed against a party that has filed an ANDA with a Paragraph IV certification. Neither Cipla nor Byron has filed an ANDA with a Paragraph IV certification against the '770 patent. Section 271(e)(2)(A) therefore does not confer jurisdiction over Prometheus's allegation that Cipla and Byron infringe the '770 patent.

D. Prometheus's Request For Leave To Amend Should Be Denied Because It Will Unduly Prejudice Roxane

Prometheus's request for leave to allege infringement of the '014 patent should be denied because adding the '014 patent to this case will prejudice Roxane.

"Courts typically find prejudice only when the amendment unfairly affects the defendants 'in terms of preparing their defense to the amendment' [and] [m]ost often, this occurs when the amended claims arise out of a subject matter different from what was set forth in the complaint and raise significant new factual issues." *Minter v. Prime Equip. Co.*, 451 F.3d 1196, 1208 (10th Cir. 2006) (quoting *Patton v. Guyer*, 443 F.2d 79, 86 (10th Cir. 1971)). As discussed above, the '770 and '014 patents concern different technologies – the '770 method of use patent claims a method of using alosetron to treat a subpopulation of female IBS patients and has U.S. inventors while the '014 process patent claims a process for making alosetron API and has U.K. inventors. Analysis of the infringement and validity of those patents will involve completely different factual inquiries.

"[A]llowing [Prometheus's] amendment would result in additional discovery, cost, and preparation" in this litigation. *See Cureton v. NCAA*, 252 F.3d 267, 273 (3d Cir. 2001). Roxane has already served discovery requests directed to Prometheus's allegations of infringement of the '770 patent and the claimed method of using alosetron, and the parties are addressing discovery disputes regarding those requests. Roxane has already subpoenaed GSK to obtain discovery relating to the '770 patent and is preparing a Hague Request, to be filed this week, to obtain '770 patent discovery from GSK in England. The parties have already exchanged infringement and invalidity contentions regarding the '770 patent and have already begun claim construction proceedings regarding the '770 patent. If Prometheus's complaint is amended, Roxane: (1) will have to draft new discovery requests directed to Prometheus's allegations of infringement of the '014 process patent for making alosetron API; (2) will likely have to serve new subpoenas on GSK; (3) will likely have to serve another Hague request to obtain discovery regarding the '014 patent from GSK and the U.K. inventors of the '014 patent; and (4) will need additional claim construction proceedings to construe the claims of the '014 patent. Roxane will also need different experts to address issues relating to the process claimed in the '014 as opposed to the method of treatment claimed in the '770 patent. All of this additional discovery threatens to delay trial of this case.

For all of the foregoing reasons, allowing Prometheus to amend its complaint would severely prejudice Roxane.

E. Prometheus's Request For Leave Should Be Denied Because Of Prometheus's Undue Delay

Prometheus's request for leave to amend its complaint should be denied because Prometheus's delay in requesting leave to amend was "undue." The sole basis for Prometheus's allegations of infringement of the '014 patent is process information produced with Roxane's ANDA. Roxane produced that information in early May 2011. Prometheus was clearly thinking about the '014 patent in mid-June when Prometheus requested discovery regarding Roxane's communications with Cipla, the manufacturing process for the alosetron API in Roxane's ANDA product, and the '014 patent. (Zullow Decl., Ex. F.) Roxane objected to producing such discovery on grounds of relevance. In response, Prometheus did not mention that it might add allegations regarding the '014 patent; instead, Prometheus simply stated that "Prometheus believes that the full scope of the limited document requests meet th[e] criteria" of being "relevant to the infringement, invalidity, or unenforceability of the '770 Patent." (Zullow Decl., Ex. G.)

Prometheus's delay in requesting leave to add allegations of infringement of the '014 patent will prejudice Roxane if the Court grants the requested leave. Prometheus knew prior to the June 3, 2011 scheduling conference that Roxane intended to take discovery from GSK entities in both the U.S. and U.K., yet waited to seek leave to amend until after Roxane served subpoenas on GSK entities in the U.S. and until shortly before the deadline for the filing of Hague Requests to obtain discovery from GSK in the U.K. Prometheus's delay precluded Roxane from efficiently obtaining discovery regarding the '770 patent and the '014 patent, and can serve no purpose but to delay resolution of this suit.

III. CONCLUSION

For the foregoing reasons, Roxane respectfully requests that Your Honor deny Prometheus's request for leave to file an amended complaint.

Respectfully yours,

/s Theodora McCormick

Theodora McCormick

Exhibits

cc: All Counsel of Record (via email)